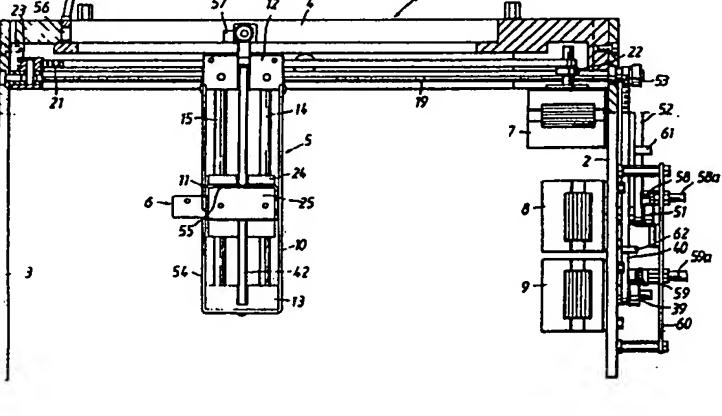


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<p>(21) International Application Number: PCT/SE91/00393</p> <p>(22) International Filing Date: 4 June 1991 (04.06.91)</p> <p>(30) Priority data: 9002000-9 5 June 1990 (05.06.90) SE</p> <p>(71) Applicant (for all designated States except US): PHARMACIA BIOSENSOR AB [SE/SE]; S-751 82 Uppsala (SE).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only) : HOLMSTRÖM, Torbjörn [SE/SE]; Nöthårvägen 53, S-752 57 Uppsala (SE). GILLE, Lars [SE/SE]; Villavägen 58, S-740 50 Alunda (SE).</p> <p>(74) Agents: WIDÉN, Björn et al.; Kabi Pharmacia AB, S-751 82 Uppsala (SE).</p>		<p>(81) Designated States: AT (European patent), BE (European patent), CH (European patent), DE (European patent), DK (European patent), ES (European patent), FR (European patent), GB (European patent), GR (European patent), IT (European patent), JP, LU (European patent), NL (European patent), SE (European patent), US.</p> <p>Published With international search report.</p>	
<p>(54) Title: LIQUID HANDLING APPARATUS</p> 			
<p>(57) Abstract</p> <p>A liquid handling apparatus comprises a frame (1) supporting an elongate horizontal member (11) and an elongate vertical member (10). The latter two are mounted to each other such that they are jointly displaceable in the transverse direction of the horizontal member (11) (X-direction) and optionally displaceable in relation to each other in the vertical direction (Z-direction) and/or in the longitudinal direction of the horizontal member (Y-direction). A liquid handling head (6) is supported by one of the horizontal member (11) and the vertical member (10) and is optionally displaceable in the longitudinal direction of the horizontal member (11). Further, there are provided X-, Y- and Z-drive motors (7, 8, 9) for displacement of the horizontal and the vertical members (11, 10) and optionally the liquid handling head (6), such that the latter may be moved in said X-, Y- and Z-directions, separately or in combinations thereof. According to the invention, the drive motors (7, 8, 9) for moving the liquid handling head (6) in the X-, Y- and Z-directions are fixedly mounted to said frame (1) and operatively connected to the respective movable members (10, 11, 6) through mechanical force transmitting means (21, 19, 42).</p>			

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LIQUID HANDLING APPARATUS

The present invention relates to an improved liquid handling apparatus capable of being used as a dosing means, 5 diluter, sampler, fractionator, or the like.

A common type of liquid handling apparatus of the above mentioned type comprises a horizontal boom member mounted above the fixed test tube rack or the like to be operated, said boom member being displaceable in the 10 transverse direction and supporting a liquid handling head for the desired function (liquid discharge, aspiration; etc) and which is displaceable along the boom member. For the apparatus to function as a sampler or autoinjector, the liquid handling head must also be movable in the vertical 15 direction, often along a vertical member supported by the boom. The movements in the different directions are normally effected by means of a separate motor for each direction of movement, usually a stepping or D.C. motor, one of the motors usually being fixedly mounted (for 20 example, for movement in the X-direction), while the other motor or motors accompany the movement in at least one direction of movement.

For example, US-A-4,422,151 discloses a liquid handling apparatus comprising a vertical mast displaceable 25 on a base plate (movement in the X-direction) and having a boom provided with a carriage which is movable along the boom (Y-direction) and supports a liquid handling tube. The latter may for vertical movement thereof (Z-direction) be supported by the carriage through a holder which is movable 30 in a vertical member. The motor for moving the boom/mast is fixedly mounted to the base plate, whereas the motor for the Y-movement is affixed to the mast and accompanies the movement thereof, and the motor for the Z-movement is carried by the above mentioned vertical member and 35 accompanies the movement of the latter.

Drive motors movably mounted as above involve several problems. Thus, the construction will of necessity be relatively unwieldy and bulky, especially since big and

heavy motors are required for moving the mass to be accelerated and retarded in the movement, this mass being increased substantially by the motors themselves. This is, of course, a disadvantage in case the liquid handling apparatus is to be built-in into or integrated with other apparatus, such as an analytical instrument. Moreover, the cabling to the movable motor(s) must be dragged along in the movements.

The object of the present invention is therefore to provide a liquid handling apparatus which is devoid of the disadvantages of the prior art apparatuses, i.e. makes possible a less bulky construction which requires smaller drive motors of lower power and which will thereby also be lighter. It will therefore be particularly well suited for incorporation into other apparatus with which it is to cooperate.

Such a liquid handling apparatus comprises (i) a frame supporting an elongate horizontal member and an elongate vertical member, said members being mounted to be jointly displaceable in the transverse direction of the horizontal member, hereinafter referred to as the X-direction, and optionally displaceable in relation to each other in the vertical direction, hereinafter the Z-direction, and/or in the longitudinal direction of the horizontal member, hereinafter the Y-direction; (ii) a liquid handling head supported by one of the horizontal member and the vertical member, and optionally displaceable in the longitudinal direction of the horizontal member; and (iii) X-, Y- and Z-drive motors for moving the horizontal and the vertical members and optionally the liquid handling head, such that the latter may be moved in the X-, Y- and Z-directions, in each direction separately or in two or three directions simultaneously in desired combinations of movements. According to the invention, the drive motors for moving the liquid handling head in the X-, Y- and Z-directions are fixedly mounted to the frame and operatively connected to the respective movable members through mechanical force transmitting means.

These force transmitting means may be of per se conventional type and may, for example, comprise endless loop means, such as chains or toothed belts, racks, screw rods, etc, or various combinations thereof.

5 In one embodiment the liquid handling apparatus has a fixed boom or bar member, along which the vertical member may be moved. The vertical member supports in turn the above mentioned horizontal member, such that the latter is vertically displaceable therealong. On the vertically 10 movable horizontal member the liquid handling head is then supported and is either rigidly mounted to the horizontal member, which in that case is displaceable in its longitudinal direction in relation to the vertical member, or is the liquid handling head displaceable along the 15 horizontal member through a carriage or slider portion movably mounted thereto.

In another embodiment the horizontal member is at one end portion thereof movably connected transversely to the boom or bar member to be displaceable along the latter in 20 its transverse direction. The vertical member is then movably mounted to the horizontal member to be displaceable therealong and carries the liquid handling head. The latter is in turn either vertically displaceable along the vertical member, or the liquid handling head is fixedly 25 mounted to the vertical member and the latter instead also vertically displaceable in relation to the horizontal member.

Preferred application-related embodiments of the 30 present liquid handling apparatus comprise apparatus designs adapted for use as, for example, sampler, fraction collector, dosing means, dispenser, autoinjector, diluter, or the like, or desired combinations thereof.

The invention will now be described in more detail with regard to a particular, non-limiting embodiment, 35 reference being made to the accompanying drawings, in which:

Fig. 1 is a front view, partially in section, of a liquid handling apparatus according to the invention;

Fig. 2 is a partial side-elevational view from the right of the apparatus in Fig. 1 with parts thereof removed;

Fig. 3 is a side-elevational view, partially in section, of the movable liquid handling apparatus in Fig 1;

Fig. 4 is a top partial view, partially in section, of the liquid handling apparatus in Fig. 1, and

Fig. 5 is a sectional view along A-A in Fig. 4.

With particular reference to Fig. 1, the apparatus illustrated in the drawings comprises a framework 1 consisting of two vertical gable or side pieces 2, 3 and a bridging bar member 4. To the latter a movable positioning unit 5 for a liquid handling head 6 is displaceably mounted, such that it may be moved along the bar member 4. To the gable piece 2 (to the right in the figure) two drive motors 8, 9, here stepping motors, are affixed, whereas a third stepping motor 7 is affixed to the bar member 4. The drive motor 7 provides for the movement of the liquid handling head 6 in the X-direction, the drive motor 8 provides for the movement in the Y-direction, and the drive motor 8 in combination with the drive motor 9 provide for the movement in the Z-direction, as will be described in more detail below.

The movable positioning unit 5 comprises, as is best shown in Figs. 3 to 5, on one hand, a vertical member 10, which at its upper part is displaceably mounted to the horizontal bar member 4 for movement therealong, and, on the other hand, a horizontal member 11, which at one end thereof is displaceably mounted to the vertical member 10 for movement up and down the latter. On the horizontal member 11 the liquid handling head 6 is in turn mounted to be horizontally displaceable along the same.

The vertical member 10 consists of an upper block 12 and a lower block 13 interconnected by two rods 14, 15. As is best shown in Fig. 4, the upper block 12 is through two horizontal bores 16, 17 therein (Fig. 3) slidably supported on rods or shaft members 18, 19 rotatably mounted in bearings in the bar member 4. The block 12 is by means of a

belt lock 20 (Fig. 4) fixed to an endless toothed belt 21, which runs between a first toothed belt wheel 22 affixed to the output shaft from the X-drive motor 7 and a second toothed belt wheel 23 rotatably journaled in bearings at 5 the opposite end of the bar member 4 (Fig. 1). By driving of the motor 7 the vertical member 10, and thereby the whole positioning unit 5, may thus be horizontally moved in the X-direction along the bar member 4.

The horizontal member 11 consists of a rear block 24 10 and a fore block 25 interconnected by two horizontal rods 26, 27. Along the latter the liquid handling head 6, which has a slider portion 28 with a sideways projecting mounting portion 29 for an injector tube or the like (not shown), is slidably mounted through two bores 30, 31 in the slider 15 portion 28.

The above mentioned rear block 24 is by means of a belt lock 32 (Fig. 5) affixed to a vertical endless toothed belt 33 which runs between a pulley 34, rotatably mounted in the lower block 13 of the vertical member 10, and a 20 toothed belt wheel 35, rotatably mounted in the upper block 12. The wheel 35 is through a centre hole 36 therein mounted to the rear horizontal rod 18 of the bar member 4 such that it is slidable along rod 18 and in rotational engagement therewith through a projection 37 provided at 25 the edge of hole 36 and received in a longitudinal groove 38 at the periphery of rod 18. By rotation of the rod 18, the horizontal member 11 with the liquid handling head 6 may thus be moved in the vertical direction (Z-direction). Such a rotation of the rod 18 is accomplished by the Z- 30 drive motor 9, the output shaft of which to that end is connected to a toothed belt wheel 39, which (Fig. 2) through a toothed belt 40 rotates a toothed belt wheel 41 affixed to the end of rod 18.

The liquid handling head 6 is for movement thereof 35 along the horizontal member 11 affixed by means of a belt lock 41 to an endless toothed belt 42, which in turn runs via a pulley 43, rotatably mounted in the fore block 25, an upper pulley 44 rotatably mounted in the rear block 24, and

further a toothed belt wheel 45 rotatably mounted in the upper block 12 of the vertical member 10. This toothed belt wheel 45 is, in corresponding manner as the toothed belt wheel 35 mentioned above, slidably mounted to the fore rod 5 19 of the bar member 4 through a centre hole 46 therein, but in rotational engagement therewith through a hole edge projection 47 cooperating with a longitudinal groove 48 at the periphery of the rod 19. From wheel 45 the toothed belt 42 runs via a pulley 49, rotatably journalled in the lower 10 block 13, and a lower pulley 50 in the rear block 24 of the horizontal member 11 back to the pulley 43. The rod 19 is rotated by means of the Y-motor 8, the output shaft of which (see Fig. 2) is connected to a toothed belt wheel 51, which through a toothed belt 52 is coupled to a toothed 15 belt wheel 53 mounted to the end of rod 19.

By the rotation of rod 19 the liquid handling head 6 may accordingly be moved along the horizontal member 11 (Y-direction). It will, however, be appreciated that the motion of the toothed belt 42 also effects a vertical 20 displacement (Z-direction) of the member 11. For a mere Y-direction movement of the liquid handling head 6 by driving of the Y-motor 8, movement in the Z-direction must therefore be prevented by locking of the Z-drive motor 9. It will likewise be appreciated that driving of the Z-motor 25 9 for movement in the Z-direction simultaneously effects a horizontal displacement of the liquid handling head 6 along the horizontal member 11. For separate movement in the Z-direction, the Y- and Z-motors must therefore be driven at the same speed and in the same direction.

30 The above described construction is suitably enclosed to a great extent by protecting covers or plates. For example, a protecting cover for the vertical member 10 is indicated by reference numeral 54 and a protecting plate for the upper part of the horizontal member 11 by reference 35 numeral 55 in Fig. 1.

Control means for operating the apparatus are not shown and will not be described specifically. However, the starting positions for the stepping motors 7-9 are defined

by fixed opto-couplers in cooperation with flags on movable members. Thus, the starting position for the stepping motor 7 is defined by an opto-coupler 56 (having a connection cable 56a) provided in the bar member 4, and a flag 57 mounted to the upper part of vertical member 10. Similarly, opto-couplers 58, 59 (with connecting cables 58a, 59a) carried by a printed circuit board 60 (which for clarity is removed in Fig. 2) cooperate with flags 61 and 62 supported by the toothed belts 52 and 40, respectively, for defining the starting points of the corresponding stepping motors 8 and 9, respectively.

When using the liquid handling apparatus as, for instance, an autoinjector, the liquid handling head 6 supports an injector tube connected to a suitable pumping equipment (not shown). A test tube rack or the like (not shown) is placed between the two gables 2, 3 in front of the vertical member 10. By suitable control of the three drive motors 7 to 9, for example through a microprocessor or the like (not shown), the liquid handling head 6 with the injector tube may then successively be brought to the various test tube positions according to the desired pattern of movement and the injector tube be immersed into the respective test tube for aspiration of liquid and transfer thereof to a desired liquid processing site, for example an analytical unit.

While the apparatus specifically described above may generally be used especially as a sampler or autoinjector, the apparatus is, by virtue of the little bulky volume, particularly suitable for being incorporated into, for example, an analytical instrument. Thus, it may, for instance, advantageously be used in apparatus like the biosensor apparatus disclosed and claimed in our previously filed international application published as WO 90/05295. It will readily be appreciated that the apparatus, even if it herein has been specifically described as an autoinjector, just as well may be used as a fraction collector, dosing means, sampler, or the like.

The invention is, of course, not restricted to the embodiment described above and specifically shown in the drawings, but many modifications and changes may be made without departing from the general inventive concept as 5 stated in the following claims.

CLAIMS

1. A liquid handling apparatus, comprising (i) a frame (1) supporting an elongate horizontal member (11) and an elongate vertical member (10) mounted to each other such that they are jointly displaceable in the transverse direction (X-direction) of the horizontal member (11) and optionally displaceable in relation to each other in the vertical direction (Z-direction) and/or in the longitudinal direction of the horizontal member (Y-direction), (ii) a liquid handling head (6) supported by one of the horizontal member (11) and the vertical member (10) and optionally displaceable in the longitudinal direction of the horizontal member (11), and (iii) X-, Y- and Z-drive motors (7, 8, 9) for displacement of the horizontal and the vertical members (11, 10) and optionally the liquid handling head (6) such that the latter may be moved in said X-, Y- and Z-directions, separately or in combinations thereof, characterized in that the drive motors (7, 8, 9) for moving the liquid handling head (6) in the X-, Y- and Z-directions are fixedly mounted to said frame (1) and operatively connected to the respective movable members (10, 11, 6) through mechanical force transmitting means (21; 18; 33; 19; 42).
2. A liquid handling apparatus according to claim 1, characterized in that said horizontal and vertical members (11, 10) are supported by a fixed horizontal bar member (4) of the upper part of said frame (1).
3. A liquid handling apparatus according to claim 2, characterized in that said bar member (4) supports an endless loop member (21) driven by the X-drive motor (7), preferably of chain or belt type, affixed to or in engagement with one of the vertical and the horizontal members (10, 11) for movement thereof in the X-direction.
4. A liquid handling apparatus according to claim 2 or 3, characterized in that the bar member (4) supports a

rotatably mounted horizontal shaft (19) driven by the Y-drive motor (8) and in rotational engagement with transmission means (42) for effecting movement of the liquid handling head (6) in the Y-direction.

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5. A liquid handling apparatus according to claim 2, 3 or 4, characterized in that the bar member (4) supports a rotatably mounted horizontal shaft (18) driven by the Z-drive motor (9) and in rotational engagement with transmission means (33) for effecting movement of the liquid handling head (6) in the Z-direction.

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6. A liquid handling apparatus according to claim 4 or 5, characterized in that said transmission means comprise endless loop means (33), preferably of chain or belt type.

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7. A liquid handling apparatus according to any one of claims 1 to 6, characterized in that the vertical member (10) is mounted to the bar member (4) to be horizontally displaceable therealong and is moved by means of the X-drive motor (7), that the horizontal member (11) is vertically displaceable along the vertical member (10) and is moved by means of the Z-drive motor (9), and that the liquid handling head (6) is displaceable along the horizontal member (11) and is moved by means of the Y-drive motor (8).

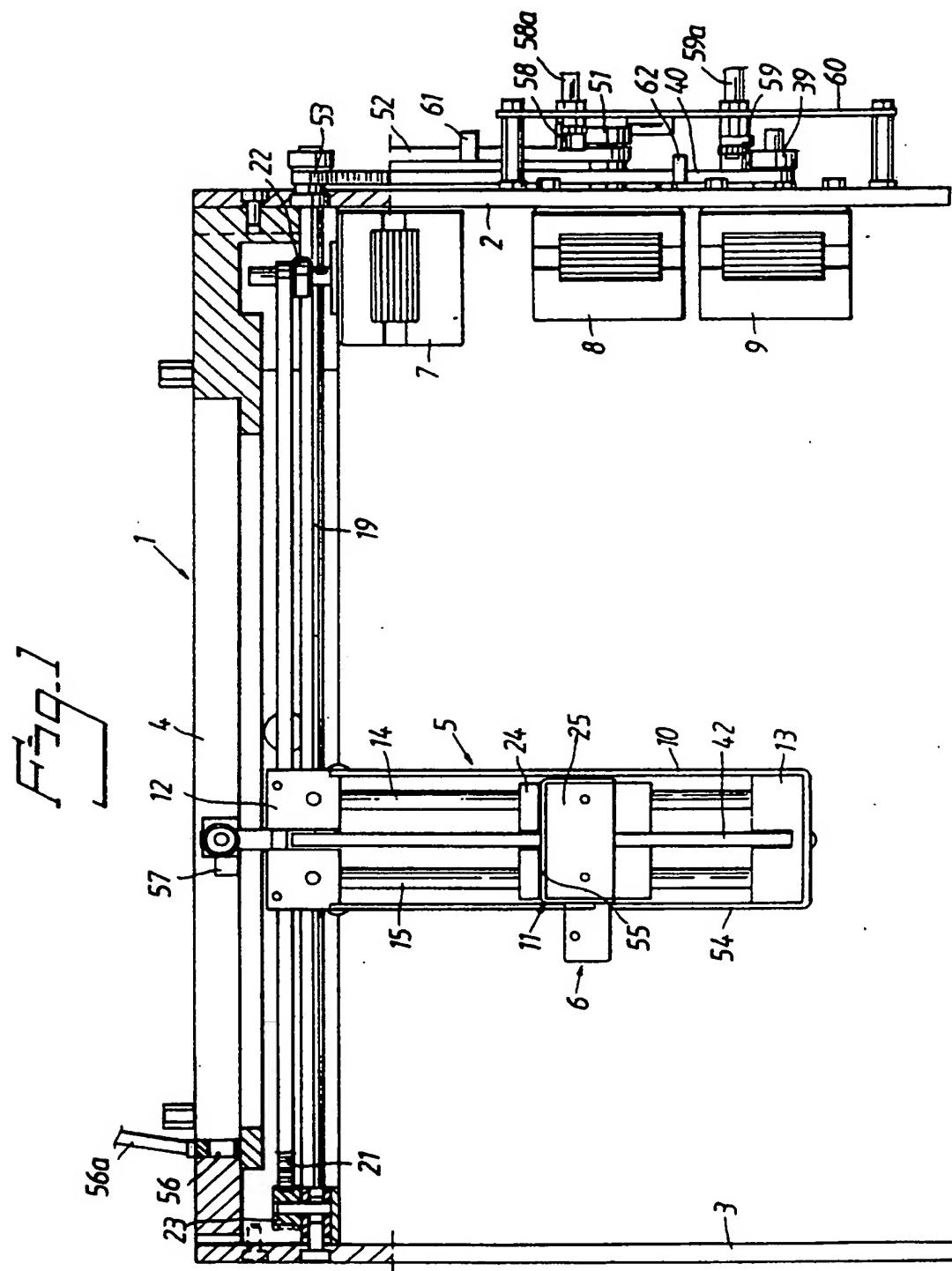
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8. A liquid handling apparatus according to claims 3 to 7, characterized in that one end of the horizontal member (11) is affixed to a first loop member (33), which runs between said rotatable rod (18) driven by the Z-drive motor (9) and a pulley (34) at the lower end (13) of the vertical member (10), that the liquid handling head (6) is affixed to a second loop member (42), which runs via said rotatable rod (19) driven by the Y-drive motor, a pulley (49) at the lower end (13) of the vertical member (10), a lower pulley (50) at the inner end (24) of the horizontal member (11), a pulley (43) at the outer end (25) of the horizontal member

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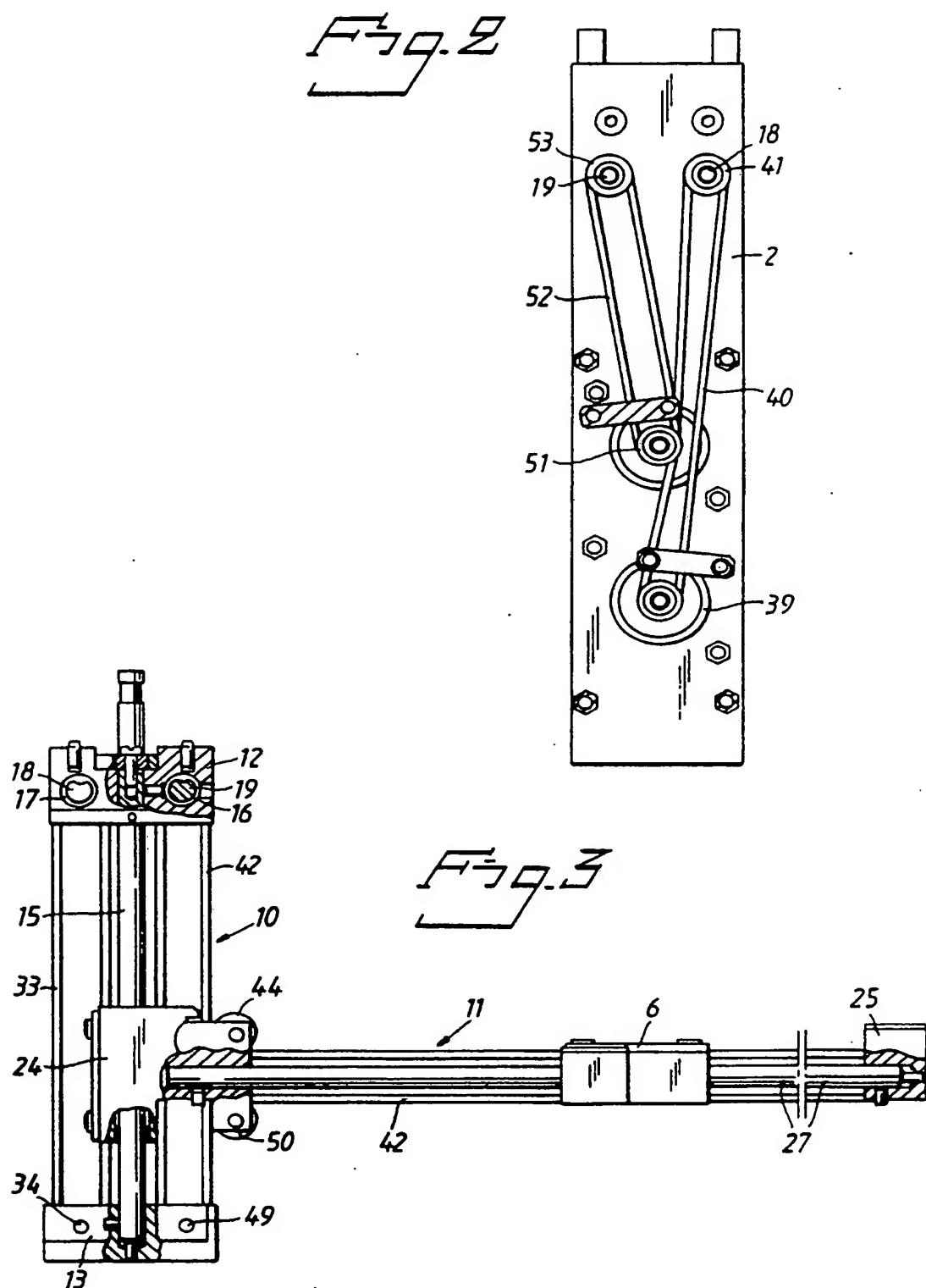
(11), and an upper pulley (44) at the inner end (24) of the horizontal member (11), and that for driving in the Y-direction, said Z-movement is locked, and for driving in the Z-direction, the Y- and Z-motors are driven at the same speed and in the same direction.

9. A liquid handling apparatus according to any one of claims 1 to 8, characterized in that it is designed for use as a sampler, fraction collector, dosing means, dispenser, autoinjector, diluter, or combinations thereof.

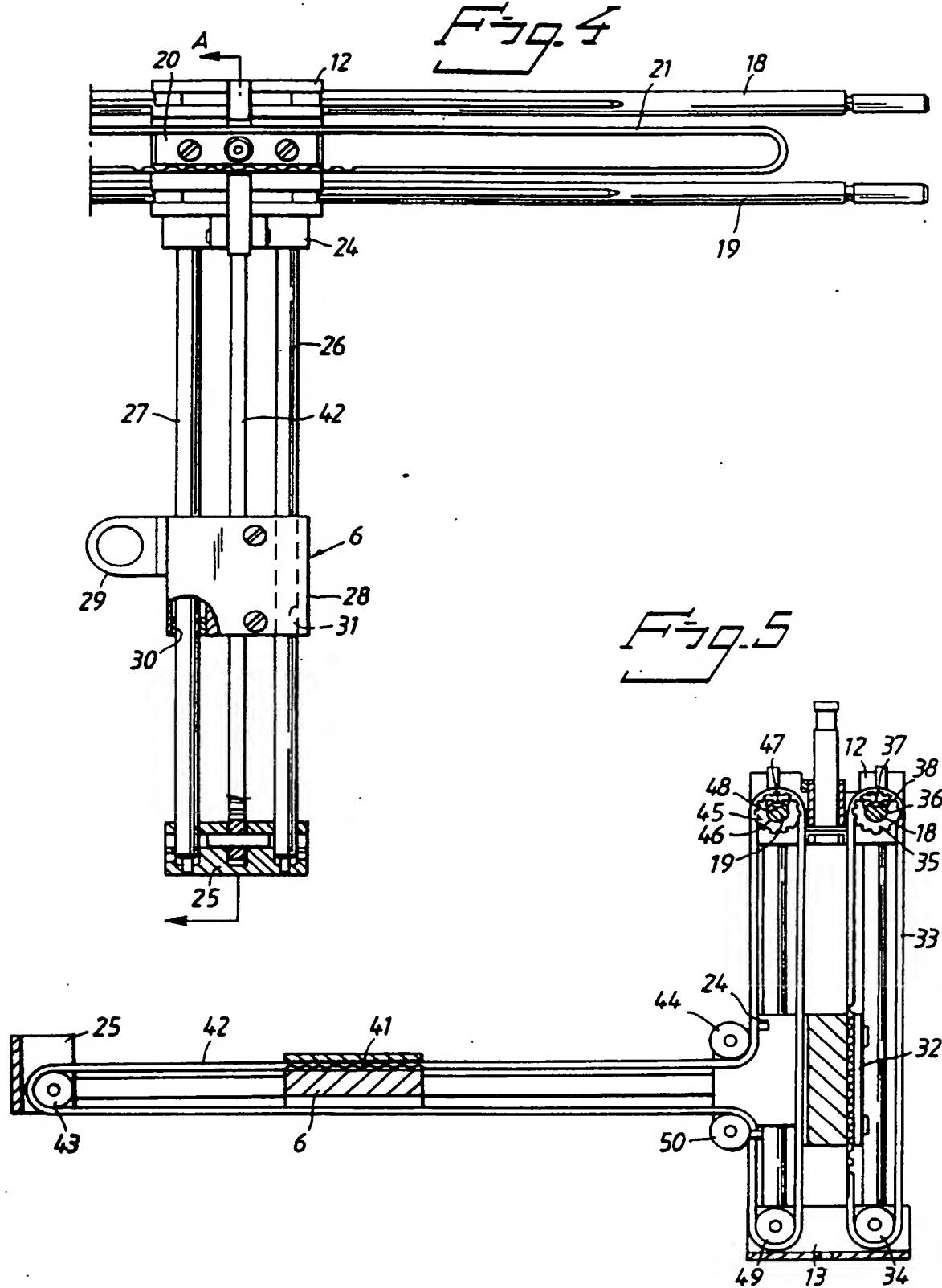


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INTERNATIONAL SEARCH REPORT

International Application No. PCT/SE 91/00393

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)⁶

According to International Patent Classification (IPC) or to both National Classification and IPC
IPC5: B 25 J 9/10

II. FIELDS SEARCHED

Minimum Documentation Searched⁷

Classification System	Classification Symbols
IPC5	B 25 J

Documentation Searched other than Minimum Documentation
to the Extent that such Documents are Included in Fields Searched⁸

SE,DK,FI,NO classes as above

III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹

Category ¹⁰	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
Y	EP, A1, 118845 (SCHLIMM) 19 September 1984, see the whole document --	1-9
Y	US, A, 4422151 (GILSON) 20 December 1983, see abstract cited in the application --	1-9
Y	WO, A1, 8302106 (HUTCHINS) 23 June 1983, see figure 2 --	1-9
Y	EP, A1, 310481 (EUDE) 5 April 1989, see abstract --	1-9
Y	EP, A1, 315310 (KEMBLE INSTRUMENT) 10 May 1989, see abstract --	1-9

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IV. CERTIFICATION

Date of the Actual Completion of the International Search

10th September 1991

Date of Mailing of this International Search Report

1991 -09- 17

International Searching Authority

Signature of Authorized Officer

SWEDISH PATENT OFFICE


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III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
Y	GB, A, 2002716 (CROUZET) 28 February 1979, see abstract --- -----	1-10

ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO.PCT/SE 91/00393

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report.
The members are as contained in the Swedish Patent Office EDP file on **91-07-31**
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Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP-A1- 118845	84-09-19	NONE		
US-A- 4422151	83-12-20	NONE		
WO-A1- 8302106	83-06-23	CA-A- 1213631 DE-T- 3249275 EP-A-B- 0095500 GB-A-B- 2123790 US-E- RE32414 US-A- 4507044	86-11-04 84-05-03 83-12-07 84-02-08 87-05-12 85-03-26	
EP-A1- 310481	89-04-05	NONE		
EP-A1- 315310	89-05-10	NONE		
GB-A- 2002716	79-02-28	DE-A- 2831361 FR-A-B- 2398347 US-A- 4218173	79-02-01 79-02-16 80-08-19	

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